New experimental drug cagrilintide (AM833), when combined with emaglutide, shows potential for treatment of obesity

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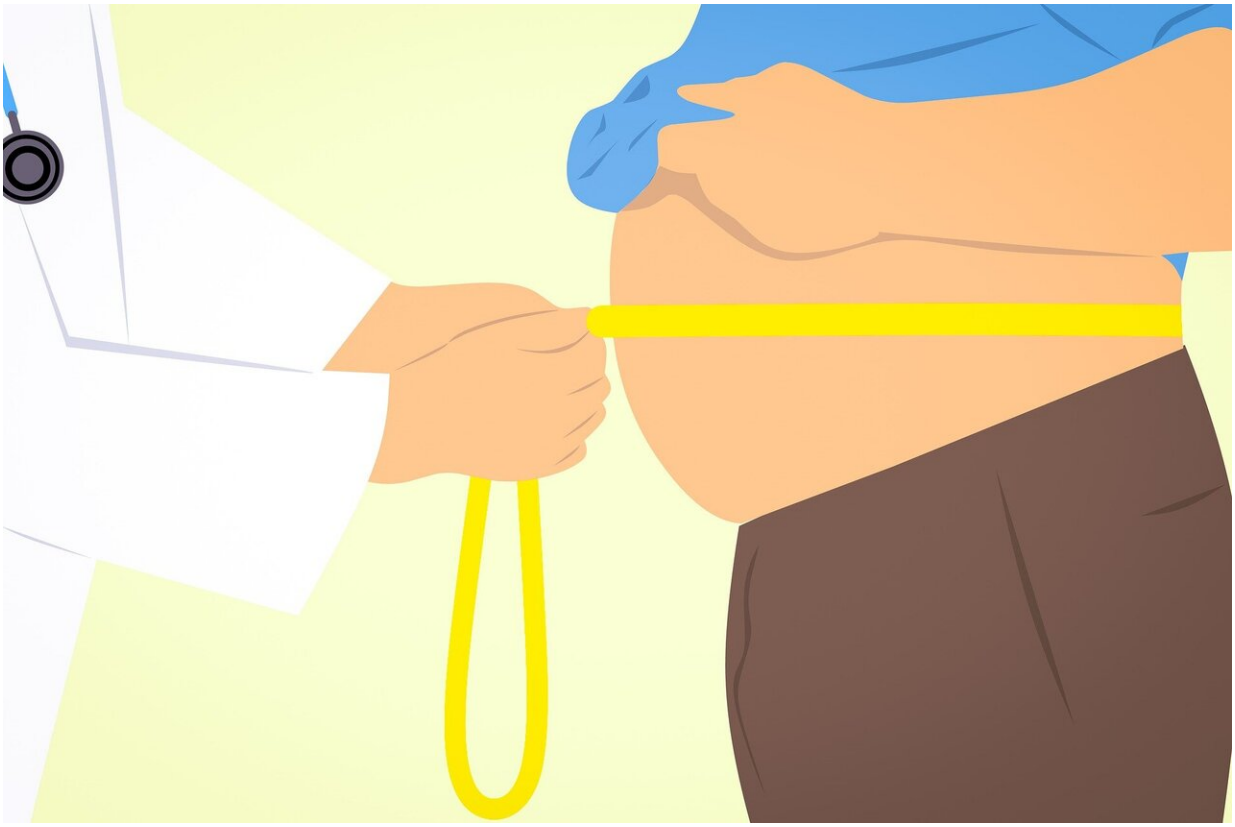

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An early study of a new experimental drug to treat obesity known as cagrilintide shows that, when combined with semaglutide 2.4 mg, the

combination leads to more weight loss than semaglutide 2.4 mg alone and is well tolerated. This phase 1 study, which was recently published in *The Lancet* will be presented at this year's European Congress on Obesity (held online, 10-13 May) by Dr. Lone Enebo, Novo Nordisk A/S, Denmark, on behalf of her colleagues. Novo Nordisk A/S is the manufacturer of both drugs in this study.

Combining medications with different modes of action may provide more effective treatment options for people with obesity. Weekly injections of cagrilintide, a newly-developed long-acting amylin analogue, in combination with semaglutide 2.4 mg, a glucagon-like peptide-1 (GLP-1) receptor agonist (already approved for type 2 diabetes), are both under clinical development for weight management. The efficacy and safety of semaglutide to treat obesity has been shown in the STEP trials, published across the past year.

This was a randomised, double-blind, placebo-controlled, phase 1 trial (NCT03600480) which took place in the U.S. to investigate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of administration of six ascending doses of weekly cagrilintide (target dose levels of 0.16, 0.3, 0.6, 1.2, 2.4, or 4.5 mg) along with semaglutide 2.4 mg versus placebo and semaglutide 2.4 mg in subjects with overweight or obesity.

The 20-week trial included a 16-week escalation period (where subjects randomised to cagrilintide received progressively increasing doses up to the target dose levels) followed by a 4-week treatment period at target dose (there were 6 different target dose levels, one per cohort: 0.16, 0.3, 0.6, 1.2, 2.4, or 4.5 mg) and a 5-week follow-up.

Eligible subjects were male or female of non-childbearing potential, due to regulatory requirements at the time of study meaning women who could potentially become pregnant were excluded. Participants of the

study were aged 18-55 years, with body mass index of between 27 and 40 kg/m^2 (ranging from having overweight to having severe obesity).

The primary endpoint was number of adverse events (AE) from baseline to follow-up. Secondary endpoints included PK of the drugs. In this early study, changes in body weight (an exploratory endpoint) were analysed separately for cagrilintide 0.16?2.4 mg + semaglutide 2.4 mg (vs pooled placebo). All participants received semaglutide 2.4 mg and ascending doses of cagrilintide or placebo.

Of 96 subjects randomised, 95 were exposed to treatment (59% male; mean age 40.6 years, body weight 95.7 kg, BMI 32.1 kg/m^2) and 80 (83%) completed the trial. The number of AEs ranged from 37-89 with cagrilintide (0.16-4.5 mg) + semaglutide 2.4 mg and 132 with placebo + semaglutide 2.4 mg. In total, there were 566 AEs reported; most AEs were mild or moderate and the proportion of subjects with 1 or more AE was similar across treatment arms.

About one-third of all AEs were gastrointestinal (GI) disorders (n=207 of 566), primarily nausea, dyspepsia, and vomiting. A greater proportion of subjects reported GI AEs with cagrilintide 1.2-4.5 mg + semaglutide 2.4 mg compared to participants receiving placebo + semaglutide 2.4 mg. The second most common AEs were injection site reactions (n=72), all mild and not dependent on cagrilintide dose.

At week 20, body weight changes from baseline with cagrilintide 1.2 and 2.4 mg + semaglutide 2.4 mg (-15.7% and -17.1%) were greater than with placebo + semaglutide 2.4 mg (?9.8%) and with cagrilintide 4.5 mg + semaglutide 2.4 mg (-15.4%) vs matched placebo + semaglutide 2.4 mg (?8.0%) with all results reaching statistical significance.

The authors conclude: "Treatment with cagrilinitide at all tested doses in combination with semaglutide 2.4 mg was generally well tolerated with

an acceptable safety profile. The data support once-weekly dosing. The combination of cagrilintide 1.2, 2.4, or 4.5 mg + semaglutide 2.4 mg led to greater weight loss compared with semaglutide 2.4 mg only."

They add: "As our data support the further clinical development of this drug combination for weight management, a phase 3 trial programme is now being planned to test cagrilinitide in combination with semaglutide for weight management."

More information: *The Lancet* (2021). www.thelancet.com/journals/lan … (21)00845-X/fulltext

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